

APPENDIX E

In the matter of an opposition by Chiron Corporation to European Patent EP 139417 (84305909.8) of Genentech Inc.

S T A T U T O R Y D E C L A R A T I O N

I, DAVID S. SECHER, do solemnly and sincerely declare as follows:

1. I am a citizen and resident of the United Kingdom.
2. I received my undergraduate training in Biochemistry from the University of Cambridge. I completed my Ph.D. in 1974, in the Medical Research Council Laboratory of Molecular Biology at the University of Cambridge under the direction of C. Milstein, an eminent immunologist and Nobel Laureate.
3. I am currently engaged as a Biotechnology Consultant and prior to this I was the director of a research effort of Celltech Ltd. In that position, I had overall responsibility for the development of novel, monoclonal antibody-based therapies.
4. I was a member of the scientific staff at the Medical Research Council Laboratory of Molecular Biology, Cambridge for thirteen years.
5. I have been on the editorial boards of Biological Reviews and Revista Biologica and am currently an editor for the journal Drug Design and Delivery.
6. I have published extensively in the broad area of immunology with specific focus on somatic mutations in antibody genes, the characterization of monoclonal antibodies, and human

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interferon. This focus naturally extends to a research interest in the prevention of viral pathogenesis and in support of this interest, I have published on research relating to papilloma, rhinovirus and Sendai virus. I have attached as an integrated appendix a list of these publications.

7. I am generally familiar with the subject matter of the above-mentioned Genentech patent, European Patent 139417 B, and with the publications of Phillip Berman and Laurence Lasky relating to their invention of a Herpes Simplex virus vaccine.

8. I am also familiar with the work reported in the references cited by the opponents.

9. As a working premise, I use the term "vaccine" in accord with the standard scientific definition. A "vaccine" protects animals against pathogenic infection by raising immunity in the animal against the pathogen. Thus, "vaccine" has the provision of protection of the animal against a pathogen by affording immunity via some component of the immune system. An entity that raises "neutralizing antibodies" is not a part of the definition of "vaccine" because raising neutralizing antibodies may be required but is certainly not itself sufficient to provide protective immunity.

10. I was asked to comment specifically on the work of Cohen et al., reported at the Eighth International Herpes Virus Workshop, Oxford, England (31 July 1983); (Reference L). For the reference to be able to support a vaccine, a definition would have to be accepted that included any substance that stimulates the production of neutralizing antibodies whether or not those

antibodies have any influence on the course of disease. The demonstration of the neutralizing antibodies was obtained from an in vitro system. There is no evidence in the reference to any benefit to animals (i.e., in vivo) in terms of protection against infection with virus or prevention of spread of the virus. Therefore, I conclude that Reference L does not enable a "vaccine" as such. (See Paragraph 9).

11. After reviewing the publications of Phillip Berman and Laurence Lasky relating to their invention of a Herpes Simplex virus vaccine, I concluded that their data was convincing. The scientific strength of this research resides in the use of a truncated version of a single glycoprotein from the rather complex model Herpes Simplex virus to confer protective immunity in the animal against the pathogen. The Berman and Lasky work provided a recombinantly produced truncated polypeptide that survived in vivo to give such protective immunity. Therefore, the Berman and Lasky results conform with the preparation of a successful vaccine that provides protective immunity in vivo against pathogenic challenge. The publication of these results provided researchers with encouragement that similar efforts would lead to success with analogous viral pathogens.

12. Further, as viruses are generally complex mosaics of various components including glycoproteins, that are arranged conformationally in a specific way, it could be supposed that this conformation is likewise required for immunoprotective antibody recognition.

13. At the time this invention was first disclosed (August

1983), one of ordinary skill in the art could not have reasonably predicted the successful preparation of an in vivo vaccine based solely on the essential presence of but one glycoprotein from the herpes simplex virus mosaic, produced as a recombinantly derived, truncated derivative that was not associated with its membrane domain.

AND I MAKE this solemn declaration, conscientiously believing the same to be true, and by virtue of the Statutory Declarations Act
1835



David S. Secher

Merlin Place Cambridge 29/1/91
place date

Before me:

C.W.C. Cheshire
SOLICITOR
G.W.A. CIMA)WICH

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